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10/067,593	02/05/2002	Lawrence Friedhoff	300.1042US	5902

7590

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DAVIDSON, DAVIDSON & KAPPEL, LLC  
14th Floor  
485 Seventh Avenue  
New York, NY 10018

EXAMINER

JIANG, SHAOJIA A.

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/067,593

**Applicant(s)**

FRIEDHOFF ET AL.

**Examiner**

Shaojia A Jiang

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This application claims priority to provisional applications Serial No. 60/265886 60/163608, 60/219435, and 60/223987.

Applicant's preliminary amendment in response to the Restriction Requirement (May 23, 2002), submitted December 29, 2003 is acknowledged, wherein Claims 17-40 have been cancelled.

Currently, claims 1-16 are pending in this application.

### ***Election/Restrictions***

Applicant's election without traverse of the invention of Group I, claims 1-16 drawn to a method for managing a patient with Alzheimer's disease or at risk of developing Alzheimer's disease, and the species of agent lovastatin, submitted December 29, 2003 is acknowledged.

On consideration by the examiner, the specie election requirement is modified to include all therapeutic agents covered by the instant claim as a single specie.

Claims 1-16 will be examined on the merits herein.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-9 and 13-16 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular agents such as HMG-COA reductase inhibitor selected from the group consisting of mevastatin, pravastatin, simvastatin, atorvastatin, lovastatin, rivastatin, fluvastatin disclosed in the specification (see page 51-59) employed in methods for treatments of Alzheimer's disease, does not reasonably provide enablement for the employment any therapeutic agent which lowers A $\beta$  levels, any HMG-COA reductase inhibitors, any NSAID, or any secretase inhibitors, or combination thereof, to be administered for the claimed methods of the particular treatments herein, i.e., Alzheimer's disease in a patient.

These recitations, "a therapeutic agent which lowers A $\beta$  levels", "an HMG-COA reductase inhibitor", a "secretase inhibitor", in these claims, are seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without **undue experimentation**. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApl's 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims;

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(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to in methods for treatments of Alzheimer's disease in a patient.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since these claims reads on any therapeutic agent which lowers A $\beta$  levels, any HMG-COA reductase inhibitors, any NSAID, or any secretase inhibitors, or combination thereof employed in the claimed methods of particular treatment herein.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants in claims 1-2, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997). The CAFC clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

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In the instant case, a therapeutic agent which lowers A $\beta$  levels", "an HMG-COA reductase inhibitor", a "secretase inhibitor" recited in the instant claims are purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides those particular compounds of formula for each kind of functional compounds for the claimed method of treatment herein (see the specification).

Thus, the instant specification fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph, since it fails to provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, except those particular compounds of formula disclosed in the specification, as discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully

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recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the claimed method of treatment herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects for treatments of Alzheimer's disease in a patient, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering to a host (e.g., a human) any compounds or their *combination* of represented by "a therapeutic agent which lowers A $\beta$  levels", or "an HMG-COA reductase inhibitor", a "secretase inhibitor", and/or while the patient also administering other medicines. See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9<sup>th</sup> ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added).

In the instant case, in the absence of fully recognizing the identity of the members genus herein except those particular compounds of formula in the specification, one of skill in the art would not be able to fully predict the possible

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treatments herein and possible adverse effects occurring with many compounds having claimed functional properties and their combinations to be administered to a host in the claimed method herein. Thus, the teachings of the "Goodman & Gilman's" book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

It is noted that only particular HMG-COA reductase inhibitor, lovastatin, is employed in working examples of the specification. Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having those functions recited in the instant claims suitable to practice the claimed invention.

*Genentech*, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test all compounds encompassed in the instant claims and their



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combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scolnick (WO 95/06470, PTO-892) in view of Applicant's admission regarding the prior art in the specification (see page 7-8).

Scolnick discloses methods of treating Alzheimer's disease or the onset of Alzheimer's disease in a human patient comprising administering to the said patient a therapeutically effective amount of a composition comprising an HMG-CoA reductase inhibitor, such as lovastatin, simvastatin, pravastatin, and fluvastatin. Scolnick also discloses that the HMG-CoA reductase inhibitor is administered by a controlled release dosage form. Note that the therapeutically effective amount of the HMG-CoA reductase inhibitor to be administered per day in the instant invention is also disclosed in Scolnick. Scolnick discloses that a drug that affects brain vasculature is useful in methods of treating Alzheimer's disease as well. See abstract, page 2 lines 16-20, page 10, and claims 1-25.

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The cited prior art does not expressly disclose the employment of the art recognized assay selected from the group consisting of radioimmunoassay, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, western blots, protein A immunoassays, and immunoelectrophoresis assays, and combination thereof, to detect A $\beta$  levels in the patient.

Applicant's admission regarding the prior art at page 7-8 of the specification teaches:

"Any procedures known in the art for the measurement of  $\beta$ -amyloid levels can be used in the practice of the instant invention. Such procedures include but are not limited to competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, western blots, protein A immunoassays, and immunoelectrophoresis assays, combinations thereof and the like." (see page 7, the 3<sup>rd</sup> paragraph, emphasis added).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the art recognized assay such as ELISA to detect A $\beta$  levels in the patient in a method of managing a patient with Alzheimer's disease.

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One having ordinary skill in the art at the time the invention was made would have been motivated to employ the art recognized assay such as ELISA to detect A $\beta$  levels in the patient in a method of managing a patient with Alzheimer's disease, since the assay herein is known in the art and art recognized as Applicant admits. Moreover, the employment of these known assay is considered well within conventional skills in the art.

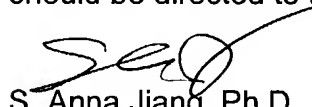
Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is 571.272.0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on 571.272.0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

  
S. Anna Jiang, Ph.D.  
Patent Examiner, AU 1617  
March 2, 2004